



# **Assessment of Prevention, Diagnosis, and Treatment Options**

**Advisory Panel Webinar**

***Friday, August 1, 2014  
2:30 – 4:30 PM (ET)***

Patient-Centered Outcomes Research Institute

# Housekeeping

- Today's webinar is open to the public and is being recorded.
  - Members of the public are invited to listen to this webinar.
  - Topic briefs and other materials are available here:  
[http://bit.ly/APwebinar\\_Aug1](http://bit.ly/APwebinar_Aug1)
  - Comments may be submitted via chat or email to [advisorypanels@pcori.org](mailto:advisorypanels@pcori.org). No public comment period is scheduled today.
- If you experience any technical difficulties, please alert us via chat or email [support@meetingbridge.com](mailto:support@meetingbridge.com).
- For those on the call, please remember to speak loudly and clearly into your phone. Please mute the lines unless you are speaking.
- Where possible, we encourage you to avoid technical language in your discussion of these topics.

# Agenda

**Welcome and Introductions**

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**Objectives and Background**

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**Discussion of Topics**

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**Closing**

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**Submitting Questions:**



Submit questions via  
the chat function in  
Meeting Bridge.

# Welcome and Introductions

# Welcome



## David Hickam, MD, MPH

Program Director  
Clinical Effectiveness Research  
PCORI

# Advisory Panel Members



# Advisory Panel Chair



## **Alvin Mushlin, MD, ScM**

Chairman, Department of Public Health,  
Weill Cornell Medical College; Public Health  
Physician-in-Chief, New York Presbyterian  
Hospital/Weill Cornell Medical Center

# Objectives and Background



# Objectives

- **Review 15 topics that had been previously discussed by the panel and prioritize these topics for further consideration as research priority areas**
- **Possible pathways for funding:**
  - Add to Pragmatic Studies funding announcement
  - Add to Single Topic Targeted funding announcement

# Criteria for reconsidering topics

Is the topic already within CER portfolio of funded awards?



Is the topic already listed as a priority topic in an existing PFA?



Does the topic have active research being conducted in the scientific community?

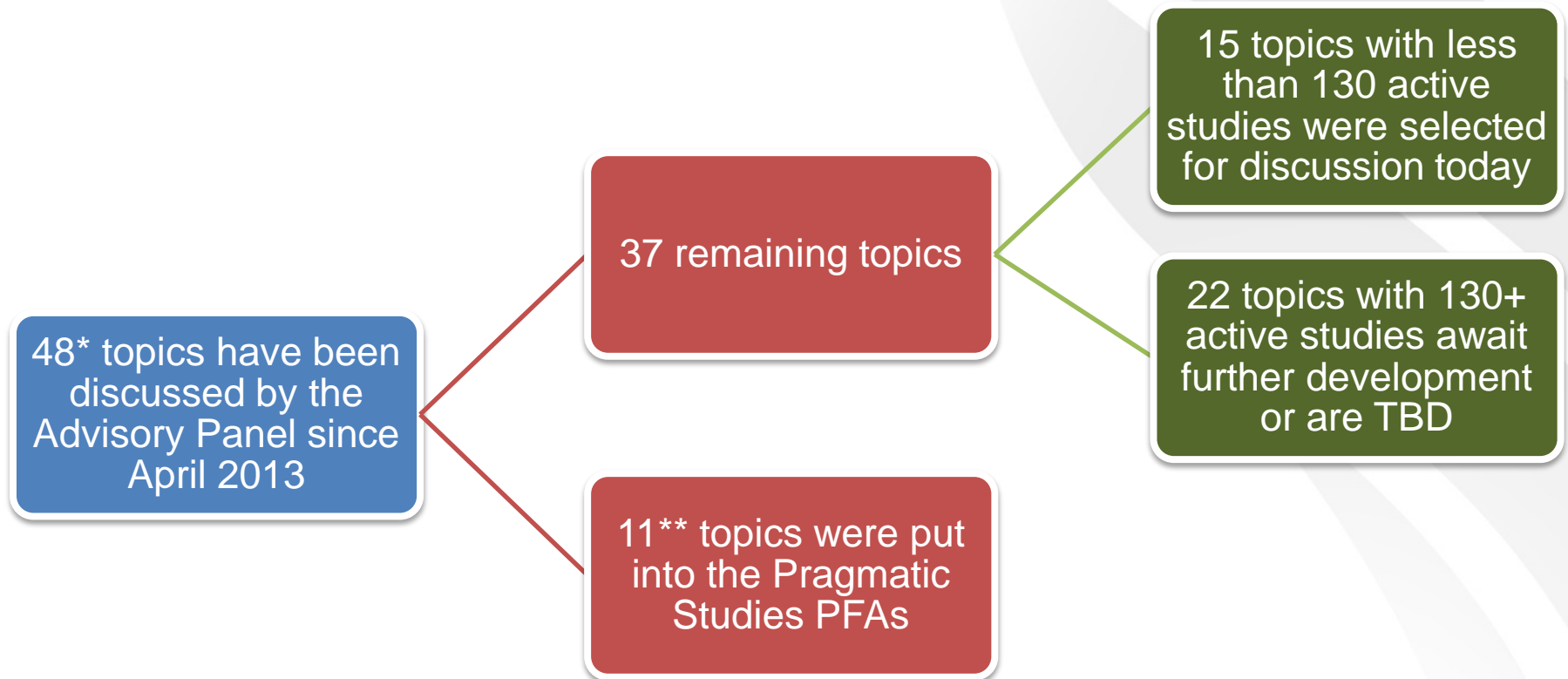
*Staff reviewed current guidance on each topic, including ongoing research on [ClinicalTrials.gov](https://clinicaltrials.gov) and [PubMed.gov](https://pubmed.gov)*

*Active studies compared to existing topic briefs to verify whether recommended options were a focus in the ongoing studies.*

# Criteria for reconsidering topics

- **PCORI intends to balance its funded portfolio to achieve synergy and avoid redundancy.**
- **Topics were removed from today's discussion if:**
  - The topic had more than 130 active studies
  - The topic was already recommended for further development or refinement.
  - The topic was closely related to a topic on the agenda for the upcoming Advisory Panel meeting on September 12.

# Pathways to prioritization



*\*Two topics were discussed twice (hearing loss and multiple sclerosis)*

*\*\*The SOC will vote on Aug. 5, 2014 on any new topic additions to the Winter 2015 Cycle of the Pragmatic Studies PFA*

# Status of prioritized topics

## April 2013 Ranking 20 Topics

- 4 topics into Pragmatic Trials PFA
- Ductal Carcinoma in Situ
  - Osteoarthritis
  - Migraine Headache
  - Bipolar Disorder

6 topics being re-reviewed today

## January 2014 Ranking 14 Topics

- 5 Topics into Pragmatic Trials PFA
- Multiple Sclerosis
  - Lung Cancer
  - Opioid Substance Abuse
  - Autism Spectrum Disorder
  - Proton Beam Therapy

5 topics being re-reviewed today

## April 2014 Ranking 16 Topics

- 2 Topics into Pragmatic Trials PFA
- Inflammatory Bowel Disease
  - Atrial Fibrillation

4 topics being re-reviewed today

# Procedures for reviewing topics and voting

## At today's meeting

- Review 15 research topics (6 minutes per topic)
- Background (1 minute)
- Panel Discussion (5 minutes)
  - *What is the important clinical question?*
  - *What are the gaps in current research?*
  - *Could research close these gaps?*
  - *How does the topic meet the 5 PCORI criteria?*

## Following today's meeting

- Participants in today's meeting will be emailed a link to Survey Gizmo ranking for completion by August 4, 2014
- Results will be shared via email to panelists within 3 days and posted online

# Discussion of Topics

# Order of discussion

9) Concussion management (April 2014)	7) Surgical options for hip fracture (April 2013)
11) Nonsurgical treatment for cervical disc and neck pain (April 2013)	8) Topical or systemic eczema in children and adults (April 2013)
1) Pelvic floor mesh implants (January 2014)	10) Arrhythmogenic right ventricular dysplasia (ARVD) (January 2014)
2) Coronary artery disease (April 2013)	12) Hypercholesterolemia in patients intolerant of statins (January 2014)
3) Early versus late bone marrow transplant treatment for children with adrenoleukodystrophy (April 2013)	13) Pemphigus vulgaris (January 2014)
4) Gestational diabetes (April 2013)	14) Mesh for the management of inguinal and abdominal hernia (January 2014)
5) Asymptomatic carotid artery stenosis (April 2013)	15) Intermittent claudication (April 2014)
6) Periodontal disease (April 2014)	



# Topic 9: Concussion management

**Overview: (1) Alan Rosenberg, (2) Linda McNamara, (3) Seema Sonnad**

- **Background:** 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.
  
- **Key points from prior discussion/topic brief:**
  - 250,000 US children were treated in 2009 for sports and recreation-related injuries that included a diagnosis of concussion or TBI.
  - Preventative possibility: should helmets be required for all sports?
  - Lack of well accepted methods for classifying the severity of the injury.
  - The treatment options need to be better defined before comparative research can be done.

# Topic 11: Nonsurgical treatment strategies in delaying or preventing surgery for cervical disc and neck pain

Overview: (1) Karen Chesbrough, (2) Denise Kruzikas, (3) Alan Rosenberg

- **Background:** 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.
  
- **Key points from prior discussion/topic brief:**
  - Lack of a concise definition of neck pain
  - No clear correlation between pain and why patients decide to seek care
  - Need better definition of patient sub-groups
  - Providers tend to choose treatments within their specialty areas.
  - Many high cost therapy options; may be efficacious to study if low cost options are just as beneficial
  - May be an opportunity for PCORI to conduct new systematic review to inform public

# Topic 1: Assessment of benefits and harms of pelvic floor mesh implants

Overview: (1) Priti Jhingran and (2) Angela Smith

- **Background:** Pelvic floor dysfunction occurs when the muscles in the pelvic floor are excessively weak or tight or there are joint problems in the surrounding area. Contributes to urinary incontinence, fecal incontinence and pelvic organ prolapse. Can be treated with surgery; mesh is sometimes inserted to provide support.
- **Key points from prior discussion/topic brief:**
  - Research could compare treatment outcomes with and without mesh.
  - Since 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.
  - Patient and provider factors may affect patient outcomes in addition to the use of mesh

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

Overview: (1) Regina Dehen and (2) James Pantelas

- **Background:** 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. 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 not on subgroups.
- **Key points from prior discussion/topic brief:**
  - Could pool trials to look at targeted subgroups
  - Possibility for some type of CER studies (stent vs. surgery, or medical therapy vs. invasive procedures vs. not intervening at all)
  - Per 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*
    - *Evaluate the CE and safety of PCI vs. CABG using existing data*

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

Overview: (1) Ronald Means, (2) Marcia Rupnow, (3) Debra Madden

- 🌐 **Background:** 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, gene therapy
  
- 🌐 **Key points from prior discussion/topic brief:**
  - How to treat rare disease as a category: may reintroduce ALD among a group of rare diseases in the next round of prioritization.
  - Better understanding of benefits, harms, and costs associated with screening for ALD in newborn males; could facilitate dietary therapy early
  - Need to define which patient subgroups benefit most from HSCT and examine outcomes
  - Research comparing less-established therapies to better established therapies in patient subgroups is needed

# Topic 4: Medical, surgical and lifestyle treatment options in the prevention and treatment of gestational diabetes

**Overview: (1) Marcia Rupnow and (2) Angela Smith**

- 🌱 **Background:** Normal pregnancy increases the body's need for insulin, resulting in increases in blood sugar. Risk of adverse outcomes for mother and infant increase. 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.
  
- 🌱 **Key points from prior discussion/topic brief:**
  - What is the research question here?
  - CER of insulin and oral agents being conducted by PhRMA
  - Benefits and harms of different behavioral strategies (diet, exercise) and drug treatments on mother and child outcomes?
  - What is the optimal management of children born to women with GDM and of women diagnosed with GDM after delivery?

# Topic 5: Medical and surgical treatment options for asymptomatic carotid artery stenosis

Overview: (1) James Pantelas, (2) Kathie Insel, (3) Debra Madden

- **Background:** 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.

- **Key points from prior discussion/topic brief:**

- Difficult to identify the patients of interest because they do not have symptoms; could screen all patients as part of a routine exam (but patients at risk may not be going to doctor)
- Need trials comparing CEA or CAS to optimal medical therapy in patients with significant asymptomatic CAD
- Need RCTs to determine if medical therapy is adequate or better compared to CEA and CAS
- Research needed on specific subgroups of patients



# Topic 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

Overview: (1) Denise Kruzikas and (2) Sara Hohly

- 🌱 **Background:** Chronic infection of the hard and soft tissue supporting the teeth. Leading cause of tooth loss in older adults. Contributes to the pathogenesis of chronic inflammation and other chronic conditions that affect general health. Treatments include medical management (eg. oral hygiene at home, root planning) and surgery (eg. flap/pocket reduction, bone grafts).
- 🌱 **Key points from prior discussion/topic brief:**
  - Few studies have provided evidence on the treatment options.
  - Prevention (improving oral hygiene) might be good focus of new research.
  - Need longitudinal studies adjusting for relevant confounding factors, such as smoking and diet, especially for highest risk populations
  - Need high quality reviews of single intervention trials and non-randomized studies, or original research directly comparing medical with surgical treatments for periodontal disease



# Topic 7: Surgical options for hip fracture in the elderly

Overview: (1) Kathie Insel and (2) Karen Chesbrough

- 🌐 **Background:** Refers to a break of the upper part of the femur (large bone of the upper thigh). Can result in pain, functional impairment, prolonged rehabilitation, loss of ability to live independently, and premature death. High variability in care.
- 🌐 **Key points from prior discussion/topic brief:**
  - May be overlap with PCORI targeted PFA and AHRQ
  - Possible widespread implementation issue re: availability of surgical intervention
  - Many areas of uncertainty involve technical issues regarding surgical management
  - Per 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*
    - *Between-class and within-class comparisons*

# Topic 8: Treatment options for topical or systemic eczema in children and adults

**Overview: (1) Cynthia Mulrow and (2) Linda McNamara**

- **Background:** Chronic inflammatory skin condition. Often first sign of allergic disease. Increasing prevalence. Significant impact on QOL, costs, and use of health care services. Standard therapy includes skin hydration, topical corticosteroids, and antihistamines.
  
- **Key points from prior discussion/topic brief:**
  - Better diagnostic methods needed
  - How to evaluate debilitating/frequent conditions (such as missed school or work)
  - 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.
  - Development and efficacy of current treatments, such as topical therapies to control itching
  - Larger trials of fish oil and/or omega-3s needed

# Topic 10: Management of arrhythmogenic right ventricular dysplasia (ARVD)

Overview: (1) Ronald Means and (2) Daniel Wall

- **Background:** Rare familial disorder in which heart muscle of right ventricle is replaced by fibrofatty tissues. Caused by mutation in genes. Usually inherited.
- **Key points from prior discussion/topic brief:**
  - ARVD is present in up to 20% of patients who die of sudden cardiac death, especially in young athletes
  - Research needed on improved diagnosis of ARVD in primary care and local settings
  - Topic briefs could not identify any systematic reviews or completed RCTs that assessed different treatment options for ARVD
  - Benefits of existing treatment options for ARVD are largely unclear due to a lack of RCT evidence

# Topic 12: Treatment options for hypercholesterolemia among patients who do not tolerate statin therapy

Overview: (1) Bettye Green and (2) Priti Jhingran

- **Background:** Statins are effective in reducing low-density lipoprotein cholesterol (LDL-c) and preventing cardiovascular events. Some people cannot tolerate statin therapy due to its adverse effects. Muscle toxicity, including myopathy and rhabdomyolysis, is statin related.
- **Key points from prior discussion/topic brief:**
  - PCOs include mortality, cardiovascular events, and muscle pain
  - Identified zero systematic reviews and six RCTs
  - Statin intolerance should be better defined. Better identification of risk factors for statin intolerance is also needed
  - Did not identify any US-based clinical practice guidelines recommending approaches to manage patients who are truly statin intolerant. Care varies for this patient population

# Topic 13: Treatment options for pemphigus vulgaris

Overview: (1) Sara Hohly and (2) Cynthia Mulrow

- **Background:** 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.
- **Key points from prior discussion/topic brief:**
  - Trials used time to no new lesions, serum antibody levels and steroid dose as primary outcome measures
  - Understanding PCOs and designing studies to measure meaningful differences in outcomes is needed
  - Most trials reported adverse effects but it is unclear if any were designed to measure differences in adverse effects between treatment groups
  - Understanding the benefits of therapies alone and in combination, as well as timing of therapies, is needed

# Topic 14: Treatment options involving mesh for management of inguinal and abdominal hernias

Overview: (1) Bettye Green and (2) Seema Sonnad

- **Background:** 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.
- **Key points from prior discussion/topic brief:**
  - Complications after surgery depends on patient factors, type of mesh used, and surgical technique; may increase with age, obesity, and other patient comorbidities
  - Comprehensive study of the different combinations in US populations is lacking
  - Studies using existing data often do not include info on type of mesh used
  - Numerous different options may limit the feasibility of RCT
  - Primary data collection for a prospective cohort study or registry may be required

# Topic 15: Treatment strategies for intermittent claudication

**Overview: (1) Daniel Wall and (2) Regina Dehen**

- **Background:** Leg pain that occurs with exertion, caused by peripheral arterial disease (PAD). Can result in poorer functional capacity, worse quality of life, and higher morbidity and mortality.
- **Key points from prior discussion/topic brief:**
  - Prevalence is on the rise
  - IOM identified this areas as top priority for CER
  - Few studies have compared current treatment options, head to head comparisons are needed
  - Often associated with comorbid conditions, so a multifactorial approach may be needed
  - Few studies include patient centered outcomes
  - Evaluation of non-pharmacologic treatments could be option for PCORI

# Pre-Meeting Ranking



# APDTO Advisory Panel Webinar, *Pre-Meeting Ranking*

Title	Score	Overall Rank
Topic 5: Carotid Artery Disease	151	1
Topic 2: Coronary Artery Disease (CAD)	148	2
Topic 11: Nonsurgical treatment for cervical disc and neck pain	129	3
Topic 4: Gestational Diabetes	129	4
Topic 7: Hip Fracture	128	5
Topic 15: Treatment strategies for intermittent claudication	125	6



# APDTO Advisory Panel Webinar, *Pre-Meeting Ranking*

Title	Score	Overall Rank
Topic 12: Treatment options for Hypercholesterolemia	109	7
Topic 6: Periodontal Disease	109	8
Topic 1: Assessment of Benefits and Harms of Pelvic Floor Mesh Implants	101	9
Topic 9: Concussion management	95	10



# APDTO Advisory Panel Webinar, *Pre-Meeting Ranking*

Title	Score	Overall Rank
Topic 8: Eczema	75	11
Topic 13: Treatment options for Pemphigus Vulgaris	73	12
Topic 3: Cerebral Adrenoleukodystrophy (ALD)	68	13
Topic 14: Treatment options involving Mesh for Management of Inguinal and Abdominal Hernias	62	14
Topic 10: Management of Arrhythmogenic Right Ventricular Dysplasia (ARVD)	58	15



Closing

# Post-discussion voting on topics

- The post-discussion Survey Gizmo ranking will be emailed to panelists immediately following this webinar. **Please complete voting by August 4, 2014.**
  - The ranking results and a brief report of today's webinar will be made available online in the next few weeks.
- Drag and drop ranking method to prioritize 15 topics
  - Topics are listed on left-hand side of screen – drag to right-hand side of screen with highest priority topic placed at the top of the list.
- Comments can be added at the end of the ranking.
- Please provide your name and click “submit” when completed.

# Next Meeting

- **In-person meeting is scheduled for Friday, September 12, 2014, from 8:00am – 5:00pm (ET)**
  - Meeting will be held in Washington, DC
  - Dinner will be hosted by the CER team on Thursday, September 11, 2014
  - Additional information will be emailed to panelists



**Thank you for your participation.**

Patient-Centered Outcomes Research Institute