

# Welcome

**Please be seated by 9:20 a.m.  
The teleconference will go live at 9:30 a.m.**



PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE



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

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## **Advisory Panel Meeting**

*July 9-10, 2015*



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# Welcome and Introductions

***David Hickam, MD, MPH***

*Program Director,  
Clinical Effectiveness Research  
PCORI*



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# Housekeeping

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- Today's teleconference is open to the public and is being recorded
  - Members of the public are invited to listen to this teleconference
  - Meeting materials can be found on the PCORI website
  - Comments may be submitted via email to [advisorypanels@pcori.org](mailto:advisorypanels@pcori.org); no public comment period is scheduled
- For those in the room, please remember to speak loudly and clearly into a microphone
- Where possible, we encourage you to avoid technical language in your discussion



# New Panel Members

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Robert Bonomo, MD



Michael Herndon, DO



Jonathan D. Klein, MD, MPH, FAAP



Leslie Levine, VMD, PhD, JD



Roy M. Poses, MD



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## Panel Member Introductions



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# Advisory Panel Chairs

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## Alvin I. Mushlin, MD, ScM

Chair, Panel on the Assessment of Options

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



## Margaret F. Clayton, RN, PhD

Co-chair, Panel on the Assessment of Options

*Associate Professor, College of Nursing and Co-Director of the PhD Program, University of Utah*



# Clinical Effectiveness Research Team

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David Hickam, MD, MPH



Yen-Pin Chiang, PhD



Harold Sox, MD



Diane Bild, MD, MPH



Anne Trontell, MD, MPH



Stanley Ip, MD



Danielle Whicher, PhD, MHS



Layla Lavasani, PhD, MHS



Julie McCormack, MA



Jana-Lynn Louis, MPH



Katie Hughes, MA



Sandi Myers



Jackie Dillard



Jess Robb, MPH



Fatou Ceesav, MPH



Kim Bailey, MS



Marina Broitman, PhD



Cary Scheiderer, PhD

# Agenda Overview

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Time	Agenda Item
9:30 – 10:00 a.m.	Welcome and Introductions
10:00 – 10:15 a.m.	Overview of the Agenda and Meeting Objectives
10:15 – 10:30 a.m.	A Tribute to Seema Sonnad
10:30 a.m. – 12:00 p.m.	Discussion: Comparative Effectiveness of Strategies for Diabetes Prevention in Prediabetes
12:00 – 1:00 p.m.	LUNCH
1:00 – 2:30 p.m.	Discussion: Comparative Effectiveness of Strategies for Diabetes Prevention in Prediabetes
2:30 – 2:45 p.m.	Break
2:45 – 4:00 p.m.	PCORI's Process for Topic Refinement
4:00 p.m.	Adjourn



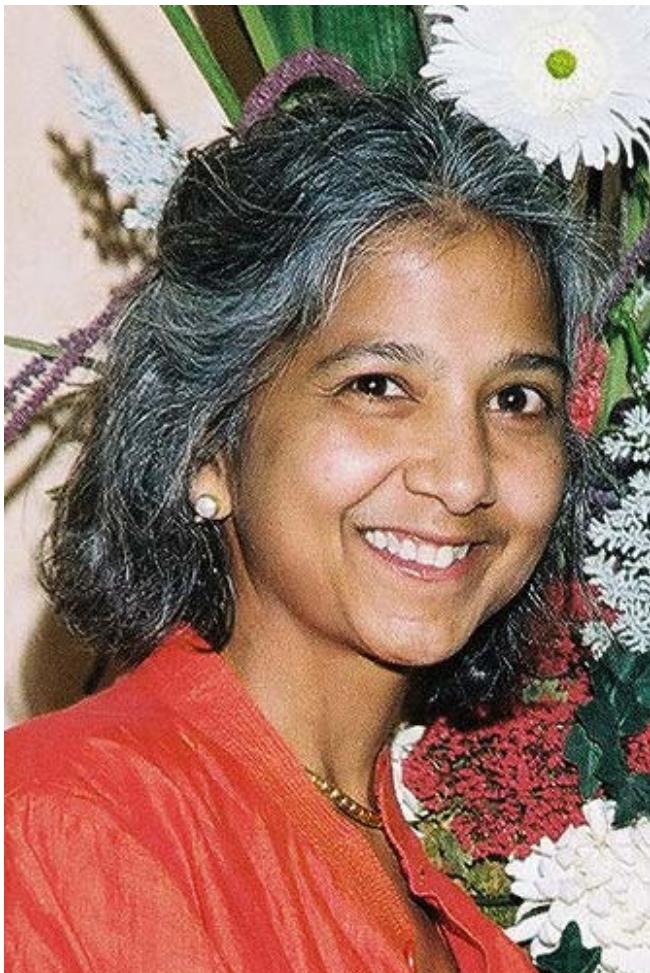
# Meeting Objective and Procedures

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- Recommend specific questions for further consideration as priority research areas
- Procedures for Reviewing Topics
  - 2 CER topics will be reviewed
    - Senior Program Officer will do 5-10 minute introduction of topic
    - Approximately 2 hour and 30 minutes discussion per topic
    - Panelists will discuss 4 or more questions per topic



# Seema Sonnad, PhD



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# Seema Sonnad, PhD



# A Memorial for Seema

The Seema S. Sonnad Ph.D. Memorial Fund for  
Young Investigators

The Value Institute, Christiana Care System

PO Box 1668

Wilmington, DE 19899



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## Topic 1:

### ***Comparative Effectiveness of Strategies for Diabetes Prevention in Prediabetes***



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# Comparative Effectiveness of Strategies for Diabetes Prevention in Prediabetes

- A large burden - 37% of the adult population have prediabetes; and this prevalence is rising
- Despite the absence of symptoms, individuals with prediabetes have poorer quality of life and a shorter life span than the population without impaired glucose
- 10% to 25% progress to diabetes within 3 years; 40% to 60% within 10 years
- Therefore, high priority should be given to research to determine the best strategies to prevent the progression of prediabetes to diabetes

# Diabetes Prevention Program (DPP) Study

- A landmark study of type 2 DM prevention in overweight patients with prediabetes
- Intensive lifestyle intervention vs. twice daily metformin + standard lifestyle intervention vs. placebo + standard lifestyle intervention
- Both interventions effective in decreasing incidence of type 2 DM but intensive lifestyle intervention was better than metformin, and remained so at 15 years
- Further research
  - Long-term outcomes (follow-up of DPP and DPP Outcomes Study)
  - Methods to sustain behavior change and weight loss
  - Examine other populations (e.g., children and youth)



# Duke Evidence Synthesis Group's Tasks

- Create a prioritized research agenda based on
  - stakeholder inputs
  - feasibility of impacting practice within the next 3 to 5 years



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# General Approach

- Appraise recent systematic reviews to identify important evidence gaps
- Transform the evidence gaps into potential research questions
- Engage relevant stakeholders to identify additional gaps and prioritize the research questions
- Cross-check potential research questions with ongoing studies

# Types of Stakeholders

- Representatives from patients and consumer advocacy groups
- Clinical experts
- Researchers
- Representatives from federal and non-federal funding agencies
- Representatives from professional societies
- Health care decision and policy makers

# Four Final CER questions (not in ranked order)

- Strategies for Implementation of Lifestyle Modification
- Different approaches to shared decision making
- Lifestyle modifications plus metformin in which population
- Different approaches to enhance adoption of preventive strategies

# Strategies for Implementation of Lifestyle Modification

- What is the comparative effectiveness of different strategies for implementing lifestyle modification (e.g., community-based approaches, primary care-based approaches, approaches that leverage communications technology, and others) in terms of program reach, patient engagement, treatment adherence/persistence, maintenance of clinical gains, feasibility of use in real-world settings, and other relevant outcomes? What elements of program delivery are associated with the best outcomes?

# Different Approaches to Shared Decision Making

- What is the comparative effectiveness of different approaches to shared decision making for selecting a diabetes prevention strategy and treatment goals (including versus provider-driven selection)? How does shared decision making affect treatment choices, treatment adherence/persistence, maintenance of clinical gains, feasibility of use in real-world settings, and other relevant outcomes? How can shared decision making facilitate the transition to an alternative diabetes prevention strategy should the initial choice prove insufficiently effective?

# LUNCH

12:30 p.m. – 1:30 p.m.



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# Lifestyle Modifications plus Metformin in Which Population

- What is the comparative effectiveness of lifestyle modification and metformin within different patient populations in terms of patient engagement, treatment adherence/persistence, maintenance of clinical gains, and other relevant outcomes? Populations of interest could be defined by demographics (e.g., age, sex, race), socioeconomic factors (e.g., insurance status, financial stress, social support), psychosocial factors (e.g., self-efficacy, comorbid mental illness), and risk for progression to diabetes (as determined by hemoglobin A1c, body mass index, or other means).

# Different Approaches to Enhance Adoption of Preventive Strategies

- What is the comparative effectiveness of different approaches (e.g., patient outreach or advertising, physician education, patient or provider incentives, and others) for enhancing utilization and adoption of diabetes prevention strategies (including both lifestyle modification and metformin) by patients, providers, and systems in real-world settings? What elements of program delivery are associated with high program utilization and adoption?



# PCORI's Process for Topic Refinement

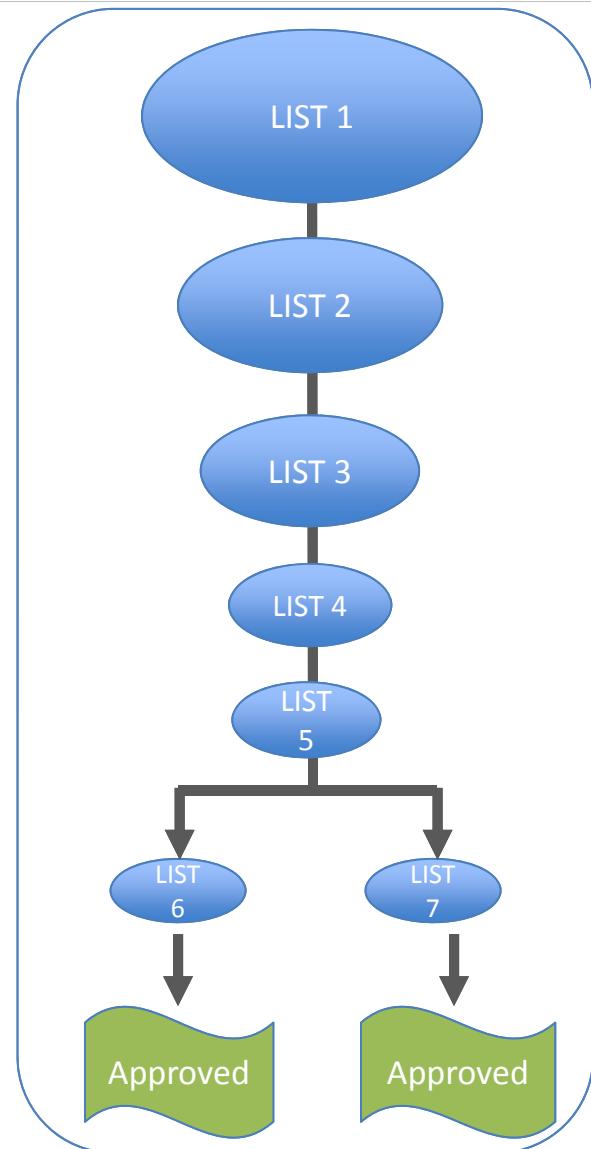
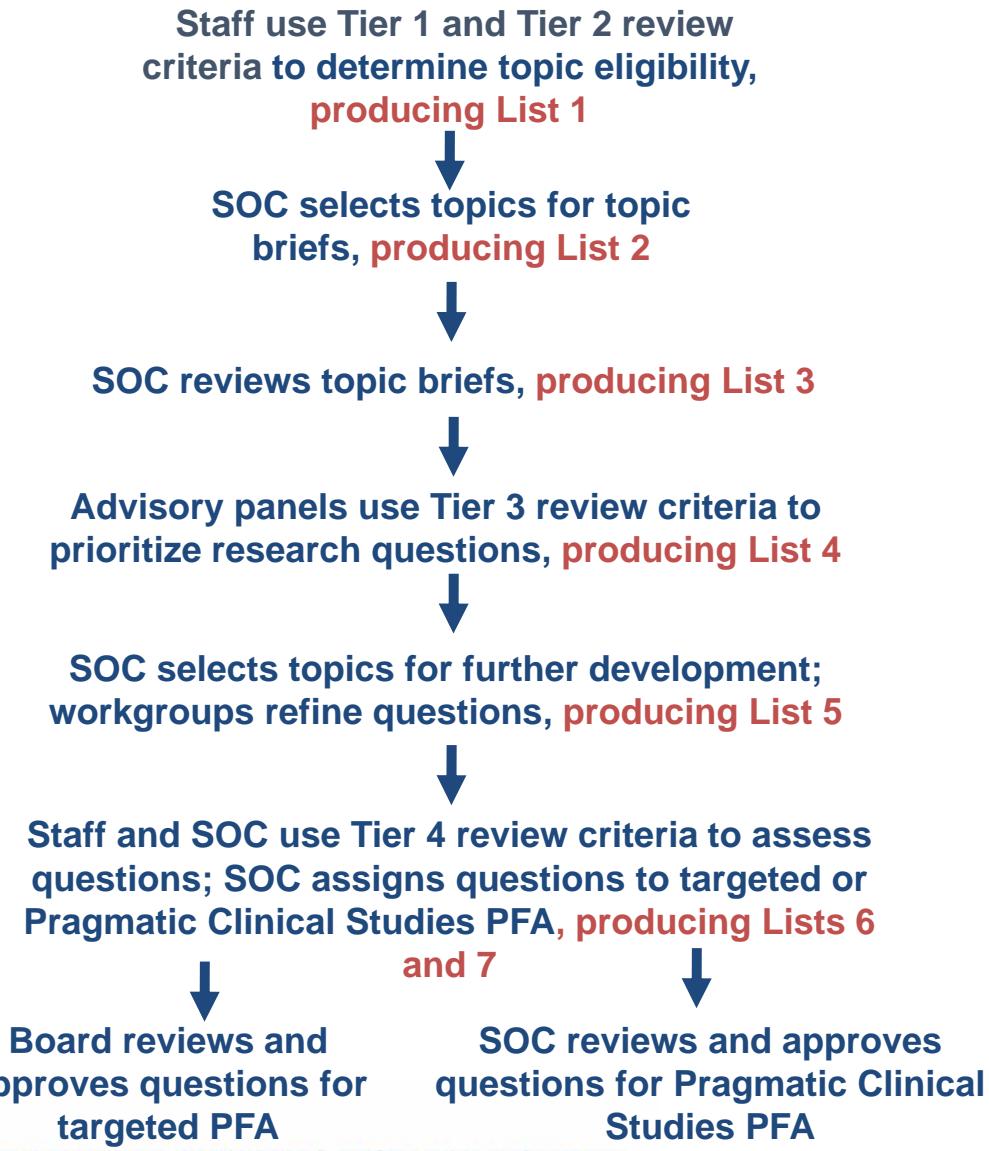


Harold Sox, MD  
Director,  
Research Portfolio Development



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# Pathway to a Funding Announcement



# Approved for Topic Brief Development

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- Insomnia
- *(New Cholesterol Control Drugs)*



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# Approved for Topic Refinement

- Comparative effectiveness of drug treatment (antihyperglycemic drugs etc.) versus non-drug treatments (weight loss/exercise) in the treatment of pre-diabetic patients. Do long-term outcomes differ across subgroups of adults?
- Comparative effectiveness of second-line drug therapies after failed metformin use (sulfonylureas, meglitinides, thiazolidinediones, acarbose, incretin agents, etc.) in type 2 diabetes treatment.
- *Future Meetings:*
  - Comparative effectiveness of narrow-spectrum antibiotics versus broad-spectrum antibiotics in the treatment of community-acquired pneumonia.
  - Compare the effectiveness of nonsurgical treatment strategies (e.g., pharmacologic treatment and physical therapy) in delaying or preventing surgery for cervical disc and neck pain.
  - Comparative effectiveness of regional plus general anesthesia versus general anesthesia alone in orthopedic procedures in terms of short- and long-term patient-centered outcomes.



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# Topic Refinement complete; awaiting next steps

- Genetic testing among children in whom a rare disease is suspected
- Mindfulness-based interventions
- ICDs in the elderly



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# Topic Refinement complete; awaiting consideration for approval for a funding announcement

- Multiple sclerosis
- Newer oral anticoagulants
- Major depression
- Management of opioid treatment of chronic pain



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# Approved for Targeted Funding Announcement

- Treatment of chronic low back pain
- High vs. low dose aspirin for secondary prevention of coronary artery disease
- Hepatitis C screening, diagnosis, and treatment



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# Topics no longer under consideration

- Statins in older people
- Monoclonal gammopathy of unknown significance
- Biomarker-guided cancer treatment
- Robotic vs. conventional treatment of gyn cancers
- Treatment of atrial fibrillation
- Surgery vs. catheter-based coronary revascularization
- IVC filter vs. anticoagulation for DVT
- Treatment of generalized anxiety disorder
- Mindfulness for anxiety, pain, and depression
- Cognitive impairment
- Breast cancer screening in high risk women
- PET vs. non-PET for monitoring cancers
- Treatment of liver cancer
- Surgery to prevent recurrence of melanoma
- Treatment of arrhythmogenic right ventricular dysplasia
- Treatment of intermittent claudication
- Treatment of diabetic retinopathy and macular degeneration
- Treatment of ADHD in children
- Treatment of PTSD
- Disease identification/risk assessment strategies for autism spectrum disorders



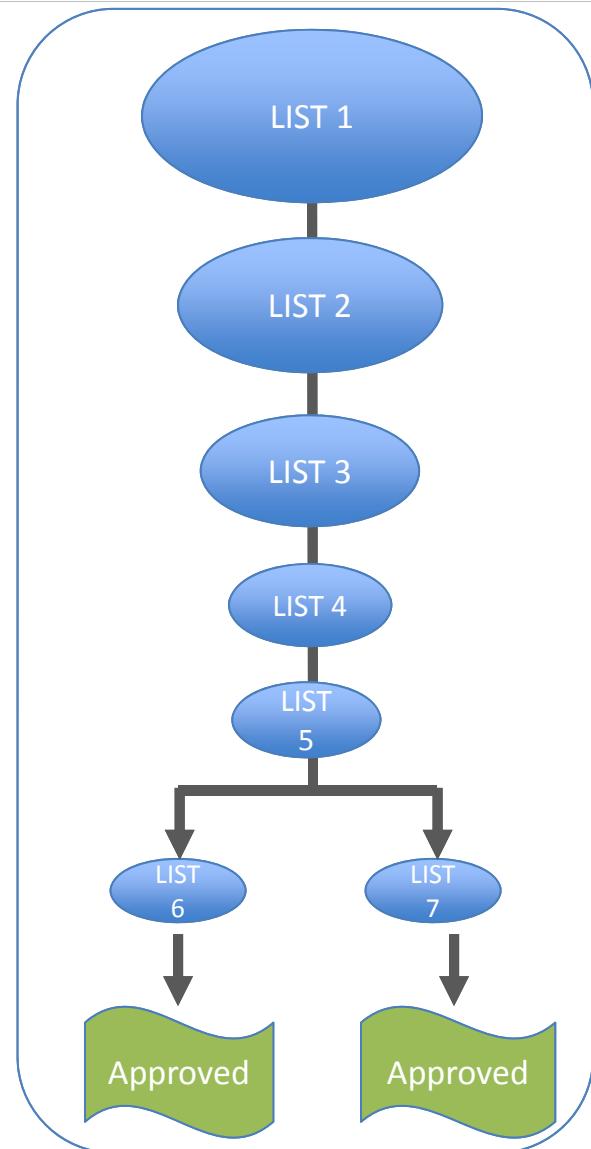
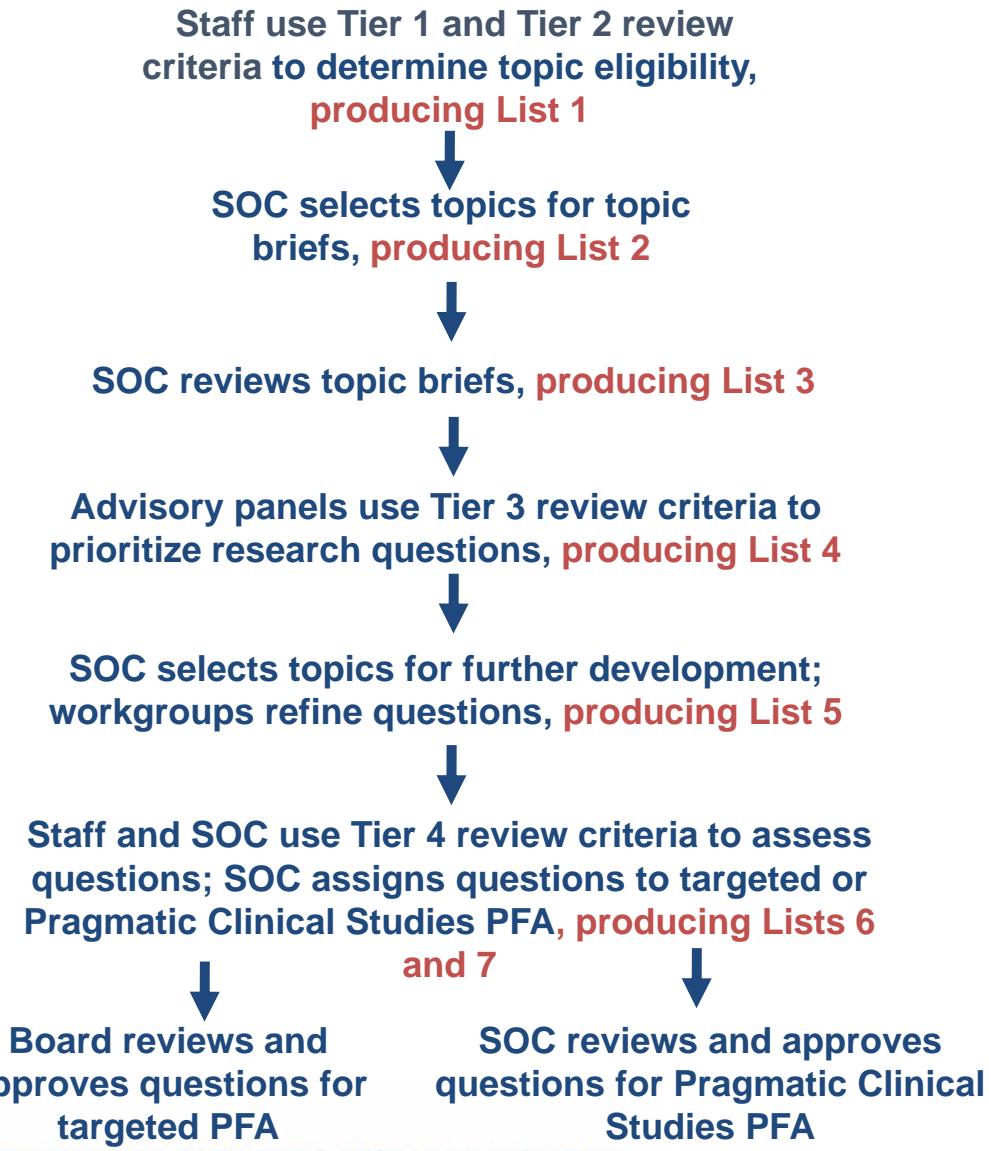
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# Topics no longer under consideration

- Management of schizophrenia
- Tests for neurocognitive impairment
- Treatment of hypercholesterolemia if statins are not tolerated
- Gestational diabetes
- Management of concussion
- Screening for intimate partner violence
- Antiretroviral drugs in the treatment of HIV infection.
- Early treatment (pre-diabetic stage) strategies versus treatment initiated after Type II diabetes
- Statin therapy for the prevention of atherosclerotic disease in patients age 70 and older
- Treatment of tendinopathies
- Treatment of epilepsy
- Treatment of Sjogren's
- BMT for adrenoleukodystrophy
- Treatment of pemphigus
- Treatment of sleep apnea
- Treatment of psoriasis
- Treatment of eczema
- Hematopoietic stem cell transplantation for older patients
- Stem cell transplantation vs immunosuppressive therapy for acquired severe aplastic anemia
- Screening options for glaucoma



# Pathway to a Funding Announcement



# PCORI website URL for the topic lists

<http://www.pcori.org/research-results/how-we-select-research-topics/generation-and-prioritization-topics-funding-4>



**Thank you for your participation.**

**Day 2 will commence at 9:00 a.m.**

**Breakfast will be available at 8:30 a.m.**

**Advisory Panel on Assessment of Prevention,  
Diagnosis, and Treatment Options**

Washington, DC

July 9-10, 2015



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# Welcome

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# Agenda Overview

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Time	Agenda Item
9:00 – 9:30 a.m.	<b>Discussion: Comparative Effectiveness of Strategies for Diabetes Prevention in Prediabetes</b>
9:30 – 11:00 a.m.	<b>Discussion: Comparative Effectiveness of Second- and Third-Line Therapies for Treatment of Type 2 Diabetes</b>
11:00 – 11:15 a.m.	<b>BREAK</b>
11:15 a.m. – 12:45 p.m.	<b>Discussion: Comparative Effectiveness of Second- and Third-Line Therapies for Treatment of Type 2 Diabetes</b>
12:45 – 1:00 p.m.	<b>Announcements and Next Steps</b>
1:00 p.m.	<b>Adjourn</b>



## Topic 1:

### ***Comparative Effectiveness of Strategies for Diabetes Prevention in Prediabetes***



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## Topic 2:

### ***Comparative Effectiveness of Second- and Third-Line Therapies for Treatment of Type 2 Diabetes***



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# Comparative Effectiveness of Second- and Third-Line Therapies for Treatment of Type 2 Diabetes

- Approximately 60% of patients with type 2 diabetes are started on metformin
- 45% of patients who initiated metformin require intensification of anti-hyperglycemic therapy within a year of first use
- Intensification includes increased dose of metformin or the need of two or more drugs to achieve adequate glycemic control.
- Clinical guidelines are not specific on optimal second- and third-line therapies
- The effects on quality of life, productivity, functional capacity, mortality and use of health care services for individuals who require second-line therapy are not well-described



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# Currently Available Second- and Third-Line Therapies

- Sulfonylureas
- Thiazolidinediones
- Dipeptidyl peptidase-4 (DPP-4) inhibitors
- Sodium-glucose cotransporter 2 (SGLT2) inhibitors
- Glucagon-like peptide-1 (GLP-1) receptor agonists
- Insulin

# Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness (GRADE) Study (Ongoing)

- Compare 4 medications commonly added to metformin
  - Glimepride (a sulfonylurea)
  - Sitagliptin (DDP-4 inhibitor)
  - Liraglutide (GLP-1 receptor agonist)
  - Glargine (long-acting insulin)
- Does not include SGLT2 inhibitors, a newer and increasingly used class of drugs
- Primary outcome: treatment failure ( $\text{HbA1c} \geq 7\%$ ) during the anticipated 4 to 7 year observation period (depending on time of entry)
- Secondary outcomes: microvascular complications, adverse effects, tolerability, quality of life, and cost-effectiveness
- Estimated enrollment is 5000 participants
- Study started in 2013; follow-up is expected to conclude in 2020



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# Duke Evidence Synthesis Group's Tasks

- Create a prioritized research agenda based on
  - stakeholder inputs
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# General Approach

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- Researchers
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# Four Final CER questions (not in ranked order)

- Different approaches to shared decision making
- Therapies in which population
- Different strategies for determining treatment success
- Approaches for enhancing diabetes treatment adherence



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# Different Approaches to Shared Decision Making

- What is the comparative effectiveness of different shared decision making approaches for choosing second- and third-line diabetes treatments in real-world settings (including versus provider-driven selection)? How do different approaches to decision making affect treatment choices, treatment adherence/persistence, diabetes control, other patient-centered outcomes (e.g., weight, hypoglycemia rates, quality of life), and maintenance of clinical gains? Are there certain aspects of diabetes treatment (e.g., medication choices, insulin use, dietary and lifestyle approaches, etc.) for which shared decision making should or should not be used?



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# Therapies in Which Population

- What is the comparative effectiveness of second- and third-line diabetes treatments for different patient populations, including those defined by demographics (e.g., age, sex, race), socioeconomic factors (e.g., insurance status, financial stress, social support), psychosocial factors (e.g., self-efficacy, comorbid mental illness), and other factors (e.g., literacy, numeracy) in terms of treatment adherence/persistence, diabetes control, other patient-centered outcomes (e.g., weight, hypoglycemia rates, quality of life), and maintenance of clinical gains? How can the choice between second-and third-line diabetes treatment options be better tailored for different populations in real-world settings?



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# **BREAK**

**11:00 a.m. – 11:15 p.m.**



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# Different Strategies for Determining Treatment Success

- What is the comparative effectiveness of different strategies for determining diabetes treatment success (for both metformin and second-/third-line treatments)? Specifically, how do treatment choices, treatment adherence/persistence, diabetes control, other patient-centered outcomes (e.g., weight, hypoglycemia rates, quality of life), and maintenance of clinical gains differ with hemoglobin A1c goal-driven decision making versus approaches that formally consider additional factors (e.g., patient values, overall diabetes complication risk, preservation of the body's ability to produce insulin, avoidance of overtreatment, and/or new technologies like continuous glucose monitoring)?



# Approaches for Enhancing Diabetes Treatment Adherence

- What is the comparative effectiveness of approaches for enhancing diabetes treatment adherence and persistence in real-world settings (for both metformin and second-/third-line treatments)? How can efficacious approaches to fostering adherence (e.g., diabetes self-management education, diabetes self-management support, treatment of comorbid mental illness, care delivery strategies that utilize communications technology to facilitate frequent contact, and approaches used in the setting of clinical trials) be feasibly implemented under real-world conditions?

# Next Steps

- Next in-person meeting will occur the week of Oct 12-16, 2015



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# Thank you for your participation

## Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options

Washington, DC  
July 9-10, 2015



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