Cycle 1 2018: Pragmatic Clinical Studies to Evaluate Patient-Centered Outcomes

Town Hall

January 29, 2018
Agenda

• Welcome
• Pragmatic Clinical Studies Funding Announcement
• Patient and Stakeholder Engagement
• Administrative Requirements
• Merit Review
• Resources
• Questions?

Submit questions via the chat function in GoToWebinar.

Ask a question via phone at the end of the presentation.
Today’s Presenters

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Pragmatic Clinical Studies
Funding Announcement
Focus on Comparative Clinical Effectiveness Research (CER)

CER includes:

- Studies that compare the clinical effectiveness, benefits, and harms of two or more approaches to health care
  - Specific treatments and procedures
  - Complex interventions intended to improve healthcare delivery

- All applicants should:
  - Explain how the research is comparative
  - Name the comparators
  - State why the comparisons are important
What is the Starting Point of Comparative Effectiveness?

• Examine the choices people make about the options for managing a disease and improving healthcare outcomes

• Consider how the need to compare these options could inform the focus of new research
  – Heterogeneity of the patient population
  – Understanding the important benefits and harms
  – Clarity about gaps in the current evidence base

• Engagement with partners facilitates these steps
What is a Pragmatic CER Study?

- Answers a practical, real world comparative effectiveness research question—a decisional dilemma
- Assesses whether two or more options differ in effectiveness when administered as they are in real life (versus tightly controlled research situations)
- The project is conducted in a clinical setting that is as close as possible to a real world setting
- Has a sufficient sample size to provide insight on heterogeneity of treatment effects
- The methodological approach (including study design, outcome measures, and follow up) is as simple as possible without sacrificing scientific rigor
Research We Do Not Fund

PCORI does not fund research whose findings will include

- cost-effectiveness analyses (CEA)
- development of clinical practice guidelines
- payment and coverage recommendations
- or policy recommendations

NOTE: PCORI does fund studies that explore the burden of costs on patients—for example, out-of-pocket costs.
PFA Overview: Pragmatic Clinical Studies to Evaluate Patient-Centered Outcomes

Objective of this PFA:

• Address critical clinical and health-related comparative effectiveness questions faced by patients, their caregivers, and their clinicians

In this PFA we seek to fund:

• Large clinical trials that use efficient approaches
• Large scale observational studies

Available Funds and Duration:

• A total of $90 million (direct and indirect) for this cycle
• Up to $10 million in total direct costs per project
• Projects should be completed within 5 years
Comparators of Interest

- Specific drugs, devices, and procedures
- Techniques for behavioral modification
- Complementary and alternative medicine
- Delivery-system interventions
Potential for the Study’s Findings to be Adopted into Clinical Practice and Improve Delivery of Care

• Describe how evidence generated from this study could be adopted into clinical practice and care delivery
  – Who are the end-users and how would the information from this study support a demand for information from end-users?
  – How likely are the findings to be reproduced by others? What are the barriers?
  – What is the dissemination plan for study results, beyond traditional publication and presentation?
• Partnership with regional and/or national partner organizations
The Case of Usual Care

• “Usual care” is typically a suboptimal comparator for CER studies.
• It is ill-defined, difficult to quantify, and subject to considerable geographic and temporal variations, thus limiting interpretability, applicability, and reproducibility.
• If the applicant proposes “usual care” as a rational and important comparator in the proposed study, then it must be described in detail, coherent as a clinical alternative, and properly justified as a legitimate comparator (e.g., usual care is guidelines-based).
• The applicant needs to address why usual care is being proposed instead of an active comparator.
• Additionally, it should be accompanied by an explanation of how the care given in the usual care group will be measured and how appropriate inferences will be drawn from its inclusion.
Justification for the Interventions that will be Studied (Including Complex Interventions)

- Should refer to existing efficacy or effectiveness studies
- Document prior evidence of efficacy or effectiveness of components of current interventions, or of effectiveness of the interventions in smaller studies or other settings
- For studies conducted in patient populations that have experienced disparities, refer to existing efficacy or effectiveness studies in the target population where possible, or highlight efficacy or effectiveness studies in the general population that may be promising for the target population
PCORI Methodology Standards

In any study, methods are critical. PCORI’s Methodology Committee developed Methodology Standards to which patient-centered CER must adhere.

The 48 standards can be grouped into 2 broad categories and 12 topic areas.

**Cross-Cutting Standards**
- Formulating Research Questions
- Patient Centeredness
- Data Integrity & Rigorous Analyses
- Preventing/Handling Missing Data
- Heterogeneity of Treatment Effects

**Design-Specific Standards**
- Data Registries
- Data Networks
- Causal Inference Methods*
- Adaptive & Bayesian Trial Designs
- Studies of Medical Tests
- Systematic Reviews
- Research Designs Using Clusters
PCS Priority Topics

- PCORI’s multi-stakeholder panels have identified 16 high-priority topics and research questions
  - First consideration will be given to applications that directly address one or more of the 16 PCORI identified topics
- Note that PCORI is open to receiving and reviewing LOIs for studies on investigator-initiated CER questions
  - AHRQ Future Research Needs Projects
  - IOM 100 priority topics for CER
- Researchers must make a strong case for the importance of the proposed research. Describe clearly the evidence gap that the study will fill.
CEDS Priority Topics

- Treatment of anxiety in children, adolescents, and young adults
- Pharmacologic, psychological, or combination treatments for treating different types of insomnia
- Alternative antibiotic regimens for empiric outpatient treatment of adults with community-acquired pneumonia
- Treatments for intermediate- or high-risk non-invasive bladder cancer who have failed first-line intravesical therapy
- Surgical treatments for acute hip fracture in elderly patients
- Treatment strategies for symptomatic osteoarthritis (OA), including joint replacement
HDDR Priority Topics

- Delivery modes for screening, Brief Intervention, and Referral to Treatment for adolescent alcohol abuse
- Multicomponent interventions to reduce initiation of tobacco use and promote cessation of tobacco use among high-risk populations with known disparities
- Integration of mental and behavioral health services into the primary care of persons at risk for disparities in health care and outcomes
- Remote delivery approaches to non-pharmacological treatments for depression and anxiety conditions
- Improving perinatal care in mothers and babies at risk for disparities
- Reducing non-traumatic lower-extremity amputations in racial or ethnic minorities and low-income populations with diabetes
- Comprehensive support services for infants and caregivers after discharge from the neonatal intensive care unit
- Alternative delivery models versus the dentist’s office in preventing dental caries in children in medically underserved areas.
- Models for integrating pharmacists into the care transitions team.
- Screening and primary prevention approaches to minimize adolescent suicidality.
What does PCORI look for when reviewing LOIs?

- Importance and relevance of the topics to PCORI priorities, as evidenced by critical gaps identified by clinical guideline developers and/or a recent relevant systematic review.
- Clarity and credibility of applicants’ responses to the LOI questions such as well-described comparators, clear research methods (e.g., study design, sample size, effect size)
- Programmatic fit and balance
Patient and Stakeholder Engagement
Patients and Other Stakeholders

PCORI Community

- Patient/Consumer
- Caregiver/Family Member of Patient
- Clinician
- Payer
- Patient/Caregiver Advocacy Org
- Hospital/Health System
- Training Institution
- Policy Maker
- Industry
- Purchaser
Patient-Centeredness vs. Patient Engagement

- **Patient-Centeredness**
  - Does the LOI mention outcomes (both benefits and harms) important to patients?
  - Are the interventions being proposed for comparison available to patients now?

- **Patient and Stakeholder engagement**
  - Does the LOI mention intent to build an interdisciplinary study team that includes appropriate patient and stakeholder representation in consultation with PCORI?
Evidence of Appropriate Engagement of Relevant Patients and Other Stakeholders

- Applicants are expected to consult with patients and other stakeholders on their decisional dilemma and evidence needs or to reference previously documented decisional dilemmas in preparation for the submission of LOIs.

- Identify the patients and stakeholders you consulted in determining that the proposed study addresses their evidentiary needs for decision-making and indicate your commitment to continuing to engage them actively in the conduct of the study.
The Engagement Rubric

The rubric is intended to provide guidance to applicants, merit reviewers, awardees, and engagement/program officers (for creating milestones and monitoring projects) regarding engagement in the conduct of research. It is divided into three segments:

1. Planning the Study
2. Conducting the Study
3. Disseminating the Study Results

PCORI Patient and Family Engagement Rubric

I. Overarching Concepts

- The rubric specifically focuses on patient and family engagement in research to help illustrate promising practices emerging in this relatively new area of engagement in research. The term “patient partners” is intended to include patients (those with lived experience), family members, caregivers, and the organizations that represent them who are representative of the population of interest in a particular study.
- Although the rubric is called the Patient and Family Engagement Rubric, there is an expectation that engagement of other stakeholders (e.g., clinicians, peers, or hospital administrators) that are relevant to a particular study will also be evaluated.
- The rubric is intended to provide guidance to applicants, merit reviewers, awardees, and engagement/program officers (for creating milestones and monitoring projects) regarding patient and family engagement in the conduct of research. It is not intended to be comprehensive or prescriptive. Instead, it provides a variety of options to incorporate engagement, where relevant, into the research process. Applicants can choose to include some, but not all, activities, and can include additional innovative approaches not listed here.
- The rubric is based on the promising practices identified in the first three rounds of PCORI awards. It is also consistent with PCORI’s Methodology Standards for patient-centeredness and its PCOR Engagement Principles.
- The rubric is structured into four sections: Planning the Study, Conducting the Study, Disseminating the Study Results, and PCOR Engagement Principles.
- The rubric provides guidance to help applicants “show their work” when describing the details of how patient and family input will be incorporated throughout the entire research process.
Budgeting

- Financial compensation of partners
- Expenses of partners (transportation, childcare, caregiver)
- Budgeting for program staff dedicated to engagement tasks
- Costs of engagement meetings and events (travel, food, audio visual)
- Additional time and resource to incorporate partner feedback into various project process
Public Posting of Partner Names

- Many members of the patient and stakeholder community have requested that PCORI make the names of partnering individuals and organizations available to credit the contributions of the full research team adequately.
- You should provide PCORI only those names of patient or stakeholder partners for whom you have obtained appropriate permission to disclose their identity to PCORI and for PCORI to use their names in public communications.
- If partners wish to remain anonymous, you may use pseudonyms or categorical descriptors (e.g., caregiver to husband with COPD, breast cancer survivor of 20 years).
- If you are selected for funding, the individuals and organizations you provided (including those described by pseudonym or categorical descriptor) will be listed on the project description page along with the other information about your project (such as abstract and PI).
Engagement Resources

• PCORI’s “The Engagement Rubric”

• Sample Engagement Plans

• Compensation Framework

• Engagement Budgeting

• Engagement in Research website page
  http://www.pcori.org/funding-opportunities/what-we-mean-engagement

• PCORI’s Methodology Standards PC-1 to PC-4
  https://www.pcori.org/research-results/about-our-research/research-methodology/pcori-methodology-standards
Administrative Requirements
Eligibility to Submit a Letter of Intent

- Any private sector (non-profit or for-profit) research organization.
- Any public sector research organization (university or college hospital or healthcare system, laboratory or manufacturer, unit of local, state, or federal government).
- Non-domestic components of organizations based in the US and foreign organizations may apply, as long as there is demonstrable benefit to the US healthcare system and US efforts in the area of patient-centered research can be clearly shown.
- Individuals are not permitted to apply.
Letter of Intent (LOI)

• An LOI is required and must be submitted prior to the deadline.

• To submit an LOI, download the PFA-specific Letter of Intent Template from the Funding Center to begin your LOI.

• You must answer all questions.

• Do not upload additional documents as part of your LOI. Letters of endorsements or support are not accepted at this stage.

• Only those LOIs deemed most responsive (programmatically and administratively) to this PFA will be invited to submit a full application.
Using the PCORI Online System

• Submit your LOI through PCORI Online: [https://pcori.force.com/engagement](https://pcori.force.com/engagement)

• Register as a New User and create your LOI as soon as possible, if appropriate

• Please note that the PI and AO cannot be the same person

• Enter information into all required fields in the system

• **PCORI Online Training Resources**
Letter of Intent (LOI)

- Download the **PCS Letter of Intent Template for this cycle** from the **Funding Center** to begin your LOI.

- LOIs must not be more than 3 pages excluding references. PCORI suggests including all references as in-text citations using American Medical Association citation style, but other citation styles are accepted. LOIs that exceed the page limit will not be reviewed.

- You must answer all questions, including the question on brief justification for the cost (“Will not exceed $10 million” is not a sufficient answer!).

- Do not upload additional documents as part of your LOI.

- Letters of endorsements or support are not accepted at this stage.

- You must upload your LOI as a PDF in PCORI Online.
Formatting

• Include the Principal Investigator’s (PI’s) full name on every page in the top left corner of the page header.

• Use at least half-inch margins and single spacing. (The header may fall within the top margin, but the body text should not begin closer than a half-inch from the edge of the page.)

• Use font size Calibri 11 for the main body of the text.

• Keep the numbering of the LOI questions within the LOI template.
Tips for Success

• Adhere to the Application Guidelines for the appropriate PFA and funding cycle
• Start and submit application early
• Have a copy of your approved LOI readily accessible
• Ensure that all team members can see the application in the system (check during the LOI stage)
• Inform your AO of your intent to submit
• Clearly describe comparators for the study
• Document evidence of efficacy/effectiveness for the intervention and comparator(s) and/or demonstrate that they are in widespread use
• Justify your power calculations based on prior evidence of anticipated effect sizes
• Clearly demonstrate the feasibility of the study
  – Show that have the team to do this and you are the right team
  – Define and support your recruitment and retention plan
  – Document that sites are already committed to participating
  – Include realistic timelines for site start-up, IRB approval, and recruitment
• Submit the completed application on/before the due date by 5:00 PM ET
Research Strategy

- **Maximum 15 pages** in length
- **Use the Research Plan Template** as your guide:
  - Specific Aims
  - Background
  - Significance
  - Study Design or Approach
- **Provide all the information requested**, as outlined in the template.
Ancillary Methodological Study (Optional)

• Provide a detailed discussion of the proposed ancillary methodological study, if applicable, which leverages opportunities in the design, execution, and analysis of the proposed large pragmatic clinical study to address important methodological issues in the context of PCOR/CER.
Research Team and Environment

• Describe the research team’s capabilities to accomplish the goals of the proposed research project and the appropriateness of the research environment to conduct the study.

• Provide all key personnel professional and partner profiles/biosketches and detailed site descriptions within the People and Places Template as a separate PDF upload.
Describe how you will make study results available to study participants after you complete the analyses.

Describe possible barriers to disseminating and implementing the results of this research in other settings.
Consortium Contractual Arrangement

- Describe the proposed components of the research project that will be performed by subcontracted organizations.
  - Explain the strengths that these partners bring to the overall project to ensure successful submission of contract deliverables in accordance with the milestone schedule.
Applicants can include additional materials that they believe are useful, but reviewers are not required to review the appendix materials in evaluating the application.
People and Places Template

Biosketch

• Required for all key personnel
  • Use NIH biosketch or PCORI’s format
  • List all partners within the Key Personnel section
• Patient and/or stakeholder biosketches

Project/Performance Site(s)

• Provide a description of the facilities that will be used during the project, including capacity, capability, characteristics, proximity, and availability to the project.
Leadership Plan Template (Dual PI application)

• Describe the governance and organizational structure of the leadership team and the research project;

• Delineate the administrative, technical, scientific, and engagement responsibilities for each PI and the rationale for submitting a dual-PI application;

• Discuss communication plans and the process for making decisions on scientific and engagement direction;

• Describe the procedure for resolving conflicts.

• Note: If this template is applicable, it should be uploaded as the first section of the People and Places Template
Letters of Support

• Letters of support should be addressed to the PI to demonstrate the commitment of key personnel and supporting organizations to the proposed project.

• Letters of support should be organized in the following manner:
  • Letters of organizational support
  • Letters of collaboration
  • Letters confirming access to patient populations, data sets, and additional resources
Milestones/Deliverables

• Milestones
  – Significant events, deliverables, tasks, and/or outcomes that occur over the course of the project that mark progress toward the project’s overall aims

• Deliverables
  – Measurable and verifiable outcomes or products that a project team must create and deliver according to the contract terms

• See Appendix 1 of the Application Guidelines for examples of milestones.
Budget

• In PCORI Online, for the Budget tab complete the following sections:
  – Detailed Research Project Budget for Each Year of the Research Project Period
  – Detailed Peer-Review Budget for Peer-Review-Related Costs
  – Budget Summary for Entire Project

• In the Templates and Uploads tab, upload the Budget Justification Template for the prime applicant and each subcontracted organization for the entire Research Project Budget and Peer-Review Budget for all research and peer-review-related costs. Include the federally negotiated or independently audited indirect cost rate letter (prime contractor) and fringe benefit rate policy verification document (prime contractor)
Using the PCORI Online System

• Navigate to PCORI Online (https://pcori.force.com/engagement)
• Log into the PCORI system early
• Please only use **Chrome, Safari, and Firefox browsers** to access the system
• The PI and the AO cannot be the same individual
• [PCORI Online Training Slides](#)
• [PCORI Online Application Cheat Sheet](#)
What happens to your application after you submit it?
Merit Review
Applicants must follow the administrative requirements stated in PCORI’s Application Guidelines.

Applications may be administratively withdrawn for the following reasons:

• Exceeding budget or time limitations
• Not using PCORI’s required templates
• Submitting incomplete sections or applications
Programmatic Screening

Applications may be programmatically withdrawn for the following reasons:

• Deviation from the approved LOI
• Inclusion of cost-effectiveness analysis (CEA)
• Inclusion of development and dissemination of clinical practice guidelines (CPG)
• Not responsive in areas listed in the PCS PFA (see pages 9-10 of PFA)
Application Review

Applications are reviewed against six criteria:

1. Study identifies critical methodological gap(s) in PCOR/CER
2. Potential for the study to improve PCOR/CER methods
3. Scientific merit
4. Investigator(s) and environment
5. Patient-centeredness
6. Patient and stakeholder Engagement

- Each application is reviewed by three scientists, one patient, and one other stakeholder
- PCORI’s Board of Governors makes funding decisions based on merit review results and program staff recommendations.
Merit Review Tips

- Address the bulleted points under each merit review criterion in the PFA
  - We refer reviewers to these bulleted points.
- Include sufficient scientific detail while making understandable to range of reviewer types
- Resubmissions
  - Reviewers see resubmission letter and previous summary statement
  - Will sometimes but not always be read by the same reviewers
  - We guide reviewers to use the merit review criteria, but also to note if applications have improved based on previous feedback.
Results of Merit Review

- Funding decisions will be announced in November 2018 with PCORI BOG meeting

- Non-Discussed Summary Statement
  - Reviewers’ written critiques

- Discussed Summary Statement
  - Reviewers’ written critiques
  - Summary of in-person discussion
  - Final overall score
Resources
Where can I find help?

**Visit pcori.org/apply**
- Application Guidelines
- FAQs
- PCORI Online User Manuals
- Sample Engagement Plans

**Schedule a Call with a Program Officer**
- Submit a request at pcori.org/content/research-inquiry
- Call 202-627-1884 (programmatic inquiries)
- E-mail sciencequestions@pcori.org

**Contact our Helpdesk**
- E-mail pfa@pcori.org
- Call 202-627-1885 (administrative and technical inquiries)
Q&A

Ask a question via the Q & A function in GOTO Meeting.

Ask a question via phone at the end of the presentation.

If we are unable to address your question during this time, e-mail the Helpdesk at pfa@pcori.org.
Thank You